Complete Summary

GUIDELINE TITLE

Use of irinotecan in the treatment of metastatic colorectal carcinoma.

BIBLIOGRAPHIC SOURCE(S)

Gastrointestinal Cancer Disease Site Group. Figueredo A, Moore M, Germond C, Kocha W, Maroun J, Zwaal C. Use of irinotecan in the treatment of metastatic colorectal carcinoma [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2000 Dec [online update]. 15 p. (Practice guideline report; no. 2-16). [20 references]

GUIDELINE STATUS

This is the current release of the guideline.

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COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Metastatic colorectal carcinoma

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To make recommendations on the use of irinotecan in the treatment of metastatic colorectal carcinoma

TARGET POPULATION

Adult patients with metastatic colorectal carcinoma for whom treatment with 5-fluorouracil has failed

INTERVENTIONS AND PRACTICES CONSIDERED

Treatment with irinotecan compared with best supportive care or 5-fluorouracil infusion regimens

MAJOR OUTCOMES CONSIDERED

Outcomes of interest were survival, time to disease progression, response rate, response duration, adverse effects, symptom improvement, and quality of life.

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Original Guideline: April 1999

A search of MEDLINE, CANCERLIT, and the Cochrane Library was conducted for the period from January 1992 to January 1999 using the subject headings "camptothecin", "colonic neoplasms", "rectal neoplasms", and "colorectal neoplasms". Information was requested from Pharmacia & Upjohn, Inc., Canada, the manufacturer of irinotecan. Roussell Laboratories provided data from two

randomized controlled trials (RCTs) relating to the adverse effects of irinotecan. Furthermore, personal reprint files, referenced articles, and proceedings of conferences, including the 1998 American Society of Clinical Oncology meeting, were reviewed. The Physician Data Query database was searched for relevant ongoing clinical trials.

December 2000 Update

The original literature search was updated using MEDLINE (through December 2000), CANCERLIT (through November 2000), the Cochrane Library (Issue 4, 2000), and the 1999 and 2000 proceedings of the annual meeting of the American Society of Clinical Oncology. The updated literature search was limited to meta-analyses and randomized trials.

Inclusion Criteria

Articles were selected for inclusion in this systematic review of the evidence is they met the following criteria:

- Articles or abstracts detailing phase II or III trials of irinotecan in patients with metastatic colorectal cancer and articles or abstracts discussing the adverse effects associated with the drug
- Only studies that reported results for the major outcomes of interest (objective response rates, duration of response or progression-free survival, adverse effects, symptom improvement, quality of life, and overall survival) were eligible for review.

NUMBER OF SOURCE DOCUMENTS

Original Guideline: April 1999

Two randomized controlled trials (RCTs), six phase II trials, and one monograph were reviewed.

December 2000 Update

New evidence has emerged on the use of irinotecan as first-line therapy for metastatic colorectal cancer. This evidence has been reviewed by the Gastrointestinal Cancer Disease Site Group (DSG) and a practice guideline on the use of irinotecan for the first-line treatment of metastatic colorectal cancer is being developed.

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Original Guideline: April 1999

A meta-analysis of efficacy data from the randomized controlled trials (RCTs) could not be conducted because irinotecan was compared with two different control regimens. However, response rates, median time to disease progression, adverse effects, and median survival times in the phase II trials were pooled using an average weighted for study population size to estimate the overall effect of irinotecan.

December 2000 Update

The information listed above remains current.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

Original Guideline: April 1999

After an intense debate about the risks, benefits, and costs of palliative chemotherapy, the Gastrointestinal Cancer Disease Site Group members agreed that irinotecan may be indicated in some patients with metastatic colorectal cancer for whom 5-fluorouracil (5-FU) chemotherapy failed. Patients must be made aware that there are significant adverse effects requiring intense supervision and adjuvant medications. Patients must also be advised that responses are usually transient but associated with improved one-year survival and quality of life, especially when compared with best supportive care (BSC). The high cost of the drug must be considered in policy development.

December 2000 Update

The information above remains current.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 26 practitioners in Ontario (26 medical oncologists). The survey consisted of items evaluating the methods, results, and interpretive summary used to inform the draft recommendations and whether the draft recommendations should be approved as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post card) and four weeks (complete package mailed again). The results of the survey were reviewed by the Gastrointestinal Cancer Disease Site Group (DSG).

Final approval of the original guideline was obtained from the Practice Guidelines Coordinating Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

After full consideration of expected benefits and harms, it is appropriate to offer treatment with irinotecan to selected patients in whom 5-fluorouracil (5-FU)-based chemotherapy has failed. The patients in whom 5-fluorouracil-based chemotherapy failed were those that progressed during palliative chemotherapy or within six months of completing adjuvant therapy. Patients should also have good performance status (2 or better) and should be able to have close medical supervision of treatment.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Original Guideline: April 1999

Two randomized controlled trials (RCTs), six phase II trials, and one monograph were reviewed. The randomized controlled trials compared irinotecan with best supportive care (BSC) or 5-fluorouracil (5-FU) infusional chemotherapy in patients for whom first-line 5-FU bolus therapy failed. Three phase II studies also presented data on chemotherapy-naïve patients.

December 2000 Update

The recommendations are supported by randomized controlled trials and phase II trials.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Irinotecan can induce objective tumour responses in approximately 15% of patients with metastatic colorectal cancer after failure of 5-fluorouracil plus leucovorin (5-FU + LV) chemotherapy. Two randomized controlled trials (RCTs), six phase II trials, and one monograph were reviewed. The RCTs used a three-week schedule of irinotecan in patients for whom treatment with 5-FU failed. Results demonstrated a significant increase in one-year survival for patients treated with irinotecan compared with patients treated with best supportive care (BSC) (36% versus 14%) or patients who were retreated with 5-FU infusion regimens (45% versus 32%). The quality of life of patients on irinotecan was better than that of patients on best supportive care but not different from that of patients on 5-FU chemotherapy.

POTENTIAL HARMS

During treatment with irinotecan, most patients experienced adverse effects, consisting of an early cholinergic syndrome, delayed diarrhea, nausea and vomiting, neutropenia, asthenia, and/or alopecia. The randomized controlled trials (RCTs) used a three-week schedule of irinotecan and detected grade 3/4 severe toxicity as follows: neutropenia in 19%, vomiting in 14%, and diarrhea in 22% of patients. Pooled results from phase II studies revealed that grade 3/4 severe toxicity included diarrhea in 33%, vomiting in 17%, and neutropenia in 38% of patients. A monograph reporting pooled data from three American phase II studies found cholinergic syndrome in 17% and asthenia in 12% of patients. Febrile neutropenia occurred in approximately 3% of patients and together with severe diarrhea accounted for a <2% treatment-related fatality rate. About 5% of patients discontinued treatment due to toxicity. More recent studies have documented lower grades of cholinergic syndrome which can be well controlled with the early use of intravenous atropine. Delayed diarrhea can be adequately controlled with the use of an intense schedule of oral loperamide. Nausea and vomiting are improved by prophylactic dexamethasone and ondansetron.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- Irinotecan is associated with serious side effects that require significant supervision and immediate treatment for severe drug-induced diarrhea and neutropenia, which occur in 22% and 19% of patients, respectively. Please see Appendix 2 of the original guideline document for recommendations on the prevention and management of adverse effects of irinotecan.
- A practice guideline on the use of irinotecan for the first-line treatment of metastatic colorectal cancer is being developed by the Gastrointestinal Cancer Disease Site Group.

- Care has been taken in the preparation of the information contained in this document. Nonetheless, any person seeking to apply or consult these guidelines is expected to use independent medical judgment in the context of individual clinical circumstances or seek out the supervision of a qualified clinician. Cancer Care Ontario makes no representation or warranties of any kind whatsoever regarding their content or use or application and disclaims any responsibility for their application or use in any way.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Gastrointestinal Cancer Disease Site Group. Figueredo A, Moore M, Germond C, Kocha W, Maroun J, Zwaal C. Use of irinotecan in the treatment of metastatic colorectal carcinoma [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2000 Dec [online update]. 15 p. (Practice guideline report; no. 2-16). [20 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Apr 30 (updated online 2000 Dec)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario
Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Provincial Gastrointestinal Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

For a current list of past and present members, please see the Cancer Care Ontario Web site.

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Gastrointestinal Cancer Disease Site Group disclosed potential conflict of interest information.

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GUIDELINE AVAILABILITY

Electronic copies: Available from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Use of irinotecan in the treatment of metastatic colorectal carcinoma. Summary. Toronto (ON): Cancer Care Ontario (CCO), 1999 Apr 30 (updated online 2000 Dec). Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.
- Browman GP, Levine MN, Mohide EA, Hayward RSA, Pritchard KI, Gafni A, et al. The practice guidelines development cycle: a conceptual tool for practice guidelines development and implementation. J Clin Oncol 1995 Feb;13(2):502-12.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on August 19, 1999. The information was verified by the guideline developer as of September 17, 1999. This NGC summary was updated by ECRI on December 3, 2001. The updated information was reviewed by the guideline developer as of January 10, 2002. This information was updated again by ECRI on May 14, 2004. The updated information was verified by the guideline developer on June 2, 2004.

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